

### AMENDMENTS

Please amend the claim as follows.

1-42. (canceled)

43. (currently amended) A method for obtaining an siRNA molecule for a target gene, wherein said siRNA molecule comprises ~~an antisense sequence that is 19—30 nucleotide bases in length and~~ a sense sequence region that is 19 – 30 nucleotide bases in length and the sense region comprises a sense sequence that is 19 bases in length ~~and said antisense sequence and said sense sequence form a duplex region of 19-30 base pairs~~, said method comprising the steps:
- (a) selecting a target gene;
  - (b) identifying a set of candidate siRNA sequences wherein each candidate siRNA comprises a sense sequence ~~wherein the antisense sequence of each of said candidate siRNA sequences is at least 79% complementary to a region of the target gene~~;
  - (c) applying to each of said candidate siRNA sequences a computer algorithm, wherein said computer algorithm comprises a set of one or more criteria selected from the group consisting of a presence of A at position 19 of the sense sequence, a presence of A at position 3 of the sense sequence, a presence of U at position 10 of the sense sequence, a presence of A at position 14 of the sense sequence, an absence of C at position 19 of the sense sequence, an absence of G at position 13 of the sense sequence, an absence of U at position 5 of the sense sequence and an absence of A at position 11 of the sense sequence, wherein said sense sequence occupies positions 1-19 of the sense region and wherein when said candidate siRNA sequence is 20-30 bases in length, bases that are within the sense region that are not within said sense sequence occupy positions 1 to 11 of the sense region and positions 1 to 11 of the sense region are immediately 5' of the 5' end of the sense sequence; a ~~presence of U at position 1 of the antisense sequence or a presence of A at a~~

~~position of the sense sequence that is complementary to position 1 of the antisense sequence, a presence of U at position 17 of the antisense sequence or a presence of A at a position of the sense sequence that is complementary to position 17 of the antisense sequence, a presence of A at position 10 of the antisense sequence or a presence of U at a position of the sense sequence that is complementary to position 10 of the antisense sequence, a presence of U at position 6 of the antisense sequence or a presence of A at a position of the sense sequence that is complementary to position 6 of the antisense sequence, an absence of G at position 1 of the antisense sequence or an absence of C at a position of the sense sequence that is complementary to position 1 of the antisense sequence, an absence of C at position 7 of the antisense sequence or an absence of G at a position of the sense sequence that is complementary to position 7 of the antisense sequence, an absence of A at position 15 of the antisense sequence or an absence of U at a position of the sense sequence that is complementary to position 15 of the antisense sequence and an absence of U at position 9 of the antisense sequence or an absence of A at a position of the sense sequence that is complementary to position 9 of the antisense sequence, wherein said positions are defined in reference to the 5' end of the antisense sequence within the duplex region;~~

- (d) after step (c) selecting a candidate siRNA sequence from the set of candidate siRNA sequences of step (b) as an siRNA sequence for the target gene, wherein said candidate siRNA sequence satisfies said set of one or more criteria; and
- (e) after step (d) synthesizing an siRNA molecule for said target gene, wherein said siRNA molecule for said target gene comprises said siRNA sequence for the target gene, whereby said siRNA molecule for said target gene is obtained.

44. (currently amended) The method according to claim 43, wherein the set of one or more criteria includes ~~the presence of U at position 1 of the antisense sequence or the presence of A at a position 19 of the sense sequence that is complementary to position 1 of the antisense sequence.~~

45. (currently amended) The method according to claim 43, wherein the set of one or more criteria includes ~~the presence of U at position 17 of the antisense sequence or~~ the presence of A at a position 3 of the sense sequence ~~that is complementary to position 17 of the antisense sequence.~~
46. (currently amended) The method according to claim 43, wherein the set of one or more criteria includes ~~the presence of A at position 10 of the antisense sequence or~~ the presence of U at a position of the sense sequence ~~that is complementary to position 10 of the antisense~~ sense sequence.
47. (currently amended) The method according to claim 43, wherein the set of one or more criteria includes ~~the presence of U at position 6 of the antisense sequence or the~~ presence of A at a position 14 of the sense sequence ~~that is complementary to position 6 of the antisense sequence.~~
48. (currently amended) The method according to claim 43, wherein the set of one or more criteria includes ~~the absence of G at position 1 of the antisense sequence or the~~ absence of C at a position 19 of the sense sequence ~~that is complementary to position 1 of the antisense sequence.~~
49. (currently amended) The method according to claim 43, wherein the set of one or more criteria includes ~~the absence of C at position 7 of the antisense sequence or the~~ absence of G at a position 13 of the sense sequence ~~that is complementary to position 7 of the antisense sequence.~~
50. (currently amended) The method according to claim 43, wherein the set of one or more criteria includes ~~the absence of A at position 15 of the antisense sequence or the~~ absence of U at a position 5 of the sense sequence ~~that is complementary to position 15 of the antisense sequence.~~

51. (currently amended) The method according to claim 43, wherein the set of one or more criteria includes ~~the absence of U at position 9 of the antisense sequence or the absence of A at a position 11 of the sense sequence that is complementary to position 9 of the antisense sequence.~~
52. (currently amended) The method according to claim 43 further comprising applying one or more additional criteria selected from the group consisting of: a GC content between about 30% and 52%, and at least 2 A or U bases at positions 11-19 ~~1-5 of the antisense sequence or at least 2 A or U bases at positions~~ of the sense sequence ~~that are complementary to positions 1-5 of the antisense sequence~~ and wherein said candidate siRNA that is selected satisfies said one or more additional criteria.
53. (currently amended) The method according to claim 43, wherein said candidate siRNA sequence that is selected as said siRNA sequence for the target gene satisfies at least two criteria selected from the group consisting of: ~~the presence of U at position 1 of the antisense sequence or the presence of A at a position 19 of the sense sequence that is complementary to position 1 of the antisense sequence, the presence of U at position 17 of the antisense sequence or the presence of A at a position 3 of the sense sequence that is complementary to position 17 of the antisense sequence, the presence of A at position 10 of the antisense sequence or the presence of U at a position 10 of the sense sequence that is complementary to position 10 of the antisense sequence, the presence of U at position 6 of the antisense sequence or the presence of A at a position 14 of the sense sequence that is complementary to position 6 of the antisense sequence, the absence of G at position 1 of the antisense sequence or the absence of C at a position 19 of the sense sequence that is complementary to position 1 of the antisense sequence, the absence of C at position 7 of the antisense sequence or the absence of G at a position 13 of the sense sequence that is complementary to position 7 of the antisense sequence, the absence of A at position 15 of the antisense sequence or the absence of U at a position 5 of the sense sequence that is complementary to position 15 of the antisense sequence, and the absence of U at position 9 of the antisense sequence or and the absence of A at a~~

position 11 of the sense sequence ~~that is complementary to position 9 of the antisense sequence.~~

54. (currently amended) The method according to claim 43, wherein said candidate siRNA sequence that is selected as said siRNA sequence for the target gene satisfies at least three criteria selected from the group consisting of: ~~the presence of U at position 1 of the antisense sequence or the presence of A at a position 19 of the sense sequence that is complementary to position 1 of the antisense sequence, the presence of U at position 17 of the antisense sequence or the presence of A at a position 3 of the sense sequence that is complementary to position 17 of the antisense sequence, the presence of A at position 10 of the antisense sequence or the presence of U at a position 10 of the sense sequence that is complementary to position 10 of the antisense sequence, the presence of U at position 6 of the antisense sequence or the presence of A at a position 14 of the sense sequence that is complementary to position 6 of the antisense sequence, the absence of G at position 1 of the antisense sequence or the absence of C at a position 19 of the sense sequence that is complementary to position 1 of the antisense sequence, the absence of C at position 7 of the antisense sequence or the absence of G at a position 13 of the sense sequence that is complementary to position 7 of the antisense sequence, the absence of A at position 15 of the antisense sequence or the absence of U at a position 5 of the sense sequence that is complementary to position 15 of the antisense sequence, and the absence of U at position 9 of the antisense sequence or the absence of A at a position 11 of the sense sequence that is complementary to position 9 of the antisense sequence.~~

55. (canceled)

56. (canceled)

57. (currently amended) The method according to claim 43, wherein in (c) said method comprises applying the following criteria to each of said candidate siRNA sequences,

~~the presence of U at position 1 of the antisense sequence or the presence of A at a position 19 of the sense sequence that is complementary to position 1 of the antisense sequence, the presence of U at position 17 of the antisense sequence or the presence of A at a position 3 of the sense sequence that is complementary to position 17 of the antisense sequence, the absence of G at position 1 of the antisense sequence or the absence of C at a position 19 of the sense sequence that is complementary to position 1 of the antisense sequence, the absence of C at position 7 of the antisense sequence or the absence of G at a position 13 of the sense sequence that is complementary to position 7 of the antisense sequence, and further comprises applying each of the following additional criteria to each of the candidate siRNA sequences: a GC content between about 30% and 52%, and at least 2 A or U bases at positions 1-5 of the antisense sequence or at least 2 A or U bases at positions 15-19 of the sense sequence that are complementary to positions 1-5 of the antisense sequence, and in (d) said siRNA sequence that is selected for said target gene satisfies the criteria of the~~  
~~presence of U at position 1 of the antisense sequence or the presence of A at a position 19 of the sense sequence that is complementary to position 1 of the antisense sequence, the presence of U at position 17 of the antisense sequence or the presence of A at a position 3 of the sense sequence that is complementary to position 17 of the antisense sequence, the absence of G at position 1 of the antisense sequence or the absence of C at a position 19 of the sense sequence that is complementary to position 1 of the antisense sequence, the absence of C at position 7 of the antisense sequence or the absence of G at a position 13 of the sense sequence that is complementary to position 7 of the antisense sequence, the GC content between about 30% and 52%, and at least 2 A or U bases at position 1-5 of the antisense sequence or at least 2 A or U bases at positions 15-19 of the sense sequence that are complementary to positions 1-5 of the antisense sequence.~~

58. (currently amended) The method according to claim 43, wherein in (c) said method comprises applying the criteria of ~~the absence of C at position 7 of the antisense sequence or the absence of G at a position 13 of the sense sequence that is complementary to position 7 of the antisense sequence~~ and further comprises

applying the criteria of a GC content of between 30% and 52% and in (d) said candidate siRNA sequence that is selected satisfies both of said criteria of: (i) the absence of C G at position 7 13 ~~of the antisense sequence or the absence of G at a position~~ of the sense sequence ~~that is complementary to position 7 of the antisense sequence~~; and (ii) the GC content of between 30% and 52%.

59. (currently amended) The method according to claim 43, wherein said candidate siRNA sequence that is selected as said siRNA sequence for the target gene satisfies each of the following criteria: the absence of G C at position 4 19 of the ~~antisense~~ sense sequence and the absence of C G at position 7 13 of the sense ~~antisense~~ sequence.

60. (currently amended) The method according to claim 43, wherein in (c), said method comprises applying the criteria of ~~the absence of C at position 7 or the absence of G at a position~~ 13 of the sense sequence ~~that is complementary to position 7 of the antisense sequence~~ and further comprises applying the criteria of a GC content of between 30% and 52%, and wherein said candidate siRNA sequence that is selected as said siRNA sequence for said target gene satisfies ~~all of the criteria of: (i) the absence of C at position 7 of the antisense sequence or the absence of G at a position~~ 13 of the sense sequence ~~that is complementary to position 7 of the antisense sequence~~; and the GC content of between 30% and 52%.

61-67 (canceled)

68. (currently amended) A method for selecting an siRNA sequence for a target gene, wherein said siRNA comprises ~~an antisense sequence that is 19–30 nucleotide bases in length and~~ a sense region sequence that is 19 – 30 nucleotide bases in length and the sense region comprises a sense sequence that is 19 bases in length and said antisense sequence and said sense sequence form a duplex region of 19–30 base pairs, said method comprising the steps:

a. (a) selecting a target gene;

- b. (b) identifying a set of candidate siRNA sequences, wherein each candidate siRNA comprises a sense sequence ~~the antisense sequence of each of said candidate siRNA sequences is at least 79% complementary to a region of the target gene;~~
- e. (c) accessing a computer and causing said computer to apply to each of said candidate siRNA sequences, a computer algorithm, wherein said computer algorithm is stored in computer readable form and comprises a set of one or more criteria selected from the group consisting of ~~a presence of U at position 1 of the antisense sequence or the~~ a presence of A at a position 19 of the sense sequence that is complementary to position 1 of the antisense sequence, a presence of U at position 17 of the antisense sequence or the ~~a presence of~~ A at a position 3 of the sense sequence that is complementary to position 17 of the antisense sequence, a presence of A at position 10 of the antisense sequence or the ~~a presence of U at a position 10 of the sense sequence that is complementary to position 10 of the antisense sequence, a presence of U at position 6 of the antisense sequence or the ~~a presence of A at a position 14 of the sense sequence that is complementary to position 6 of the antisense sequence, an absence of G at position 1 of the antisense sequence or the~~ an absence of C at a position 19 of the sense sequence that is complementary to position 1 of the antisense sequence, an absence of C at position 7 of the antisense sequence or the ~~an absence presence of G at a position 13 of the sense sequence that is complementary to position 7 of the antisense sequence, an absence of A at position 15 of the antisense sequence or the~~ an absence of U at a position 5 of the sense sequence that is complementary to position 15 of the antisense sequence and an absence of U at position 9 of the antisense sequence or ~~and the absence of A at a position 11 of the sense sequence that is complementary to position 9 of the antisense sequence, wherein said sense sequence occupies positions 1-19 of the sense region and wherein when said candidate siRNA sequence is 20-30 bases in length, bases that are within the sense region that are not within said sense sequence occupy positions 1 to 11 of the sense region and positions 1 to 11 of the sense region are immediately~~~~



~~5' of the 5' end of the sense sequence said positions are defined in reference to the 5' end of the antisense sequence within the duplex region;~~

- ~~d.~~ (d) after step (c) selecting a candidate siRNA sequence from the set of candidate siRNA sequences of step (b) as said siRNA sequence for the target gene, wherein said candidate siRNA sequence satisfies said set of one or more criteria, and wherein said selecting is performed by said computer; and
- ~~e.~~ (e) after step (d) generating an output comprising said siRNA sequence for the target gene, wherein said generating is performed by said computer and said output is displayed in a form that is readable by a human.

69. (canceled)

70. (currently amended) The method according to claim 68, wherein the set of one or more criteria includes ~~the presence of U at position 1 of the antisense sequence or the presence of A at a position 19 of the sense sequence that is complementary to position 1 of the antisense sequence.~~

71. (currently amended) The method according to claim 68, wherein the set of one or more criteria includes ~~the presence of U at position 17 of the antisense sequence or the presence of A at a position 3 of the sense sequence that is complementary to position 17 of the antisense sequence.~~

72. (currently amended) The method according to claim 68, wherein the set of one or more criteria includes ~~the presence of A at position 10 of the antisense sequence or the presence of U at a position 10 of the sense sequence that is complementary to position 10 of the antisense sequence.~~

73. (currently amended) The method according to claim 68, wherein the set of one or more criteria includes ~~the presence of U at position 6 of the antisense sequence or the presence of A at a position 14 of the sense sequence that is complementary to position 6 of the antisense sequence.~~

74. (currently amended) The method according to claim 68, wherein the set of one or more criteria includes ~~the absence of G at position 1 of the antisense sequence or the absence of C at a position 19 of the sense sequence that is complementary to position 1 of the antisense sequence.~~
75. (currently amended) The method according to claim 68, wherein the set of one or more criteria includes ~~the absence of C at position 7 of the antisense sequence or the absence of G at a position 13 of the sense sequence that is complementary to position 7 of the antisense sequence.~~
76. (currently amended) The method according to claim 68, wherein the set of one or more criteria includes ~~the absence of A at position 15 of the antisense sequence or the absence of U at a position 5 of the sense sequence that is complementary to position 15 of the antisense sequence.~~
77. (currently amended) The method according to claim 68, wherein the set of one or more criteria includes ~~the absence of U at position 9 of the antisense sequence or the absence of A at a position 11 of the sense sequence that is complementary to position 9 of the antisense sequence.~~
78. (canceled)
79. (currently amended) The method according to claim 43, wherein in (b) said sense ~~antisense~~ sequence is ~~100% complementary to said~~ the same as a region of said target gene.
80. (canceled)

81. (currently amended) The method according to claim 68, wherein in (b) said sense antisense sequence is ~~100% complementary to said~~ the same as a region of said target gene.

82. (canceled)

83. (canceled)

84. (previously presented) The method according to claim 43, wherein said synthesizing comprises chemical synthesis.

85. (previously presented) The method according to claim 43, wherein said synthesizing comprises enzymatic synthesis.

86. (currently amended) A method for obtaining an siRNA molecule for a target gene, wherein said siRNA molecule comprises ~~an antisense sequence that is 19–30 nucleotide bases in length and~~ a sense sequence that is 19 – 30 nucleotide bases in length and the sense region comprises a sense sequence that is 19 bases in length and ~~said antisense sequence and said sense sequence form a duplex region of 19–30 base pairs,~~ said method comprising the steps:

- a. selecting a target gene;
- b. identifying a set of candidate siRNA sequences, wherein each candidate siRNA comprises a sense sequence ~~the antisense sequence of each of said candidate siRNA sequences is at least 79% complementary to a region of the target gene;~~
- c. applying to each of said candidate siRNA sequences a computer algorithm, wherein said computer algorithm comprises a set of four or more criteria selected from the group consisting of: ~~the presence of U at position 1 of the antisense sequence or the~~ a presence of A at a position 19 of the sense sequence that is complementary to position 1 of the antisense sequence, the

~~presence of U at position 17 of the antisense sequence or the~~ a presence of A  
~~at a position 3 of the sense sequence that is complementary to position 17 of~~  
~~the antisense sequence, the presence of A at position 10 of the antisense~~  
~~sequence or the~~ a presence of U at a position 10 of the sense sequence that is  
~~complementary to position 10 of the antisense sequence, the presence of U at~~  
~~position 6 of the antisense sequence or the~~ a presence of A at a position 14 of  
~~the sense sequence that is complementary to position 6 of the antisense~~  
~~sequence, the absence of G at position 1 of the antisense sequence or the~~ an  
~~absence of C at a position 19 of the sense sequence that is complementary to~~  
~~position 1 of the antisense sequence, the absence of C at position 7 of the~~  
~~antisense sequence or the~~ an absence of G at a position 13 of the sense  
~~sequence that is complementary to position 7 of the antisense sequence, the~~  
~~absence of A at position 15 of the antisense sequence or the~~ an absence of U  
~~at a position 5 of the sense sequence that is complementary to position 15 of~~  
~~the antisense sequence, the absence of U at position 9 of the antisense~~  
~~sequence or the~~ an absence of A at a position 11 of the sense sequence that is  
~~complementary to position 9 of the antisense sequence, a GC content between~~  
~~about 30% and 52%, and at least 2 A or U bases at positions 1-5 of the~~  
~~antisense sequence or at least 2 A or U bases at positions 15-19 of the sense~~  
~~sequence that are complementary to positions 1-5 of the antisense sequence,~~  
~~wherein said positions are defined in reference to the 5' end of the antisense~~  
~~sequence within said duplex region~~ wherein said sequence occupies positions  
1-19 of the sense region and wherein when said candidate siRNA sequence is  
20-30 bases in length, bases that are within the sense region that are not  
within said sense sequence occupy positions 1 to 11 of the sense region and  
positions 1 to 11 of the sense region are immediately 5' of the 5' end of the  
sense sequence;

- ~~d.~~ (d) after step (c) selecting a candidate siRNA sequence from the set of  
candidate siRNA sequences of step (b) as an siRNA sequence for the target  
gene, wherein said candidate siRNA sequence satisfies said set of four or  
more criteria; and

- e. (e) after step (d) synthesizing said siRNA molecule for said target gene, wherein said siRNA molecule for said target gene comprises said siRNA sequence for the target gene, whereby said siRNA molecule for said target gene is obtained.

87. (currently amended) The method according to claim 86, wherein in (c) said method comprises applying a set of five or more criteria selected from the group consisting of: ~~the presence of U at position 1 of the antisense sequence or the presence of A at a position 19 of the sense sequence that is complementary to position 1 of the antisense sequence, the presence of U at position 17 of the antisense sequence or the presence of A at a position 3 of the sense sequence that is complementary to position 17 of the antisense sequence, the presence of A at position 10 of the antisense sequence or the presence of U at a position 10 of the sense sequence that is complementary to position 10 of the antisense sequence, the presence of U at position 6 of the antisense sequence or the presence of A at a position 14 of the sense sequence that is complementary to position 6 of the antisense sequence, the absence of G at position 1 of the antisense sequence or the absence of C at a position 19 of the sense sequence that is complementary to position 1 of the antisense sequence, the absence of C at position 7 of the antisense sequence or the absence of G at a position 13 of the sense sequence that is complementary to position 7 of the antisense sequence, the absence of A at position 15 of the antisense sequence or the absence of U at a position 5 of the sense sequence that is complementary to position 15 of the antisense sequence, the absence of U at position 9 of the antisense sequence or the absence of U at a position 11 of the sense sequence that is complementary to position 9 of the antisense sequence,~~ a GC content between about 30% and 52%, and at least 2 A or U bases at ~~positions 1-5 of the antisense sequence or at least 2 A or U bases at positions 15-19 of the sense sequence that are complementary to positions 1-5 of the antisense sequence,~~ and wherein in (d) said candidate siRNA sequence that is selected as said siRNA sequence for said target gene satisfies said set of five or more criteria.